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NP9 1RH

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I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

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Dated 29th January. 1999.

Patents Form 1/77

Patents Act 1977
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P01/7700 25.00 - 9800370.0

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

8 JAN 1998

The Patent Office
Cardiff Road
Newport
Gwent NP9 1RH

1. Your reference

DCW/VSW

2. Patent application number
(The Patent Office will fill in this)

9800370.0

0 8 JAN 1998

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

Diametrics Medical Limited
Short Street
High Wycombe
Buckinghamshire HP11 2QH

Patents ADP number *(if you know it)*

7193345001

If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention

Method & apparatus for monitoring cerebral physiology

5. Name of your agent *(if you have one)*

Brookes & Martin

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

High Holborn House
52/54 High Holborn
London WC1V 6SE

Patents ADP number *(if you know it)*

471001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*

a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
See note (d))

YES

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	
Description	7
Claim(s)	2
Abstract	
Drawing(s)	2

10. If you are also filing any of the following, state how many against each item.

Priority documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application.

Signature Brookes & Martin Date 8 January, 1998

BROOKES & MARTIN

12. Name and daytime telephone number of person to contact in the United Kingdom

0171 242 9631 - David C. Woodcraft

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Notes

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METHOD & APPARATUS FOR MONITORING CEREBRAL PHYSIOLOGY

This invention relates to a method and apparatus for monitoring the cerebral cellular environment, especially in patients who have sustained brain injury.

In the event of medical incidents, such as severe trauma to the head, it is frequent practice to monitor the intracranial pressure (ICP) in a ventricle of the brain. An increase in ICP is thought to be indicative of secondary injury such as brain swelling, and it is known to be necessary to relieve pressure by draining cerebrospinal fluid (CSF) if a patient's ICP rises above a critical level. While a body of data exists in the management of intracranial hypertension there have been few investigations of the significance of other cerebral physiological parameters.

The present invention is based on this observation that the pH of CSF is an indicator of the condition of a patient's brain after suffering head trauma and thus the likely outcome of medical treatment.

According to one aspect of the present invention there is provided a method of predicting the outcome of head trauma which comprises monitoring the pH of cerebrospinal fluid (CSF) and comparing the measured pH with a base line representing brain death.

In investigations which have been carried out by the present inventors, a pH sensor was inserted into a cerebral ventricle of a patient and the pH monitored by sequential measurements. Both the rate of change of pH and the absolute level of pH were measured on a continuous basis. While a rapid decrease of pH is a strong indicator of a poor survival prognosis, the absolute value of pH can be used directly to provide a guide to the patients' well being. In general, it has been found that stable levels of pH in the region of 7.15 to 7.25 suggest that the patient is likely to improve clinically, while significantly lower pH levels or continuously falling pH levels are a pointer to poor survival chances. In one case, a pH of about 7.05 correlated with brain stem death.

The present invention also includes apparatus for monitoring the pH and optionally other cerebral physiological parameters which comprises a lumen adapted for introduction through an opening in a skull of a living patient into a cerebral ventricle, said lumen having a pH sensor therein and permitting CSF to flow thereinto and over the sensor.

Preferably, the pH sensor contains a pH-sensitive colour change or fluorescent material and the colour change or fluorescence is measured optically by determining the absorption of a standard light beam.

The catheter containing the pH probe may be a single lumen and may also be used for removing samples of CSF fluid from the ventricle. Alternatively, a bi-lumen catheter may be employed in which the sensor is housed in one lumen and CSF is withdrawn from the other lumen. Removal of CSF may be desirable because of a perceived increase in ICP or may be removed prior to a detected increase in ICP because of a predicted deterioration in the patient's well being because of a fall in pH.

The invention is illustrated by reference to the accompanying drawings in which:-

Figure 1 is a section through a tubular probe containing various sensors;

Figure 2 is a part section through the probe;

Figure 3 is a schematic view showing one way in which the apparatus may be connected to a patient;

Figure 3A is an enlarged view of the Luer lock; and

Figure 3B is a partial section through the patient's head showing one method of introducing the lumen containing the pH sensor.

Referring to the drawings the apparatus comprises a tubular probe (1) comprising a microporous sheath which permits the transfer of CSF into a gel (A) filling the probe. A number of sensors are housed within the tubular probe. One of these is a pH sensor (3). Sensor 3

catheter. The distal tip of the catheter is provided with holes to permit flow of CSF therethrough and around the tip of the probe which is also located within the cerebral ventricle.

Example

16 patients admitted to hospital following brain trauma resulting in severe brain injury (GCS $\leq$ 8) were included in the study. A 'Paratrend 7' sensor measuring pH, pCO_2 and pO_2 was advanced into a ventriculostomy. Sensor data was stored into a computer and transferred to a spreadsheet, pH, pCO_2, pO_2, 1CP, CPP, patent manipulation and outcome were monitored.

Six patients were excluded due to technical difficulties in obtaining and recording data early in the study.

Four patients were found to have initial pH in the range 7.15 to 7.22 but had progressive CSF acidemia over the next 24 to 48 hours. All progressed to herniation and brain death. Clinical evidence of brain death occurred as the pH approached 7.05.

Two patients were found to have a relative high initial CSF pH in the range 7.20-7.25. These values remained substantially constant and both patients remained vegetative.

In the remaining four patients initial pH was in the range 7.12 to 7.24 but increased over the following 48 hours. All displayed significant clinical recovery.

It was found that patient care activities and other known stressors were found to cause a rapid decrease in CSF pH which resolved shortly after the activity stopped. All negative changes in brain pH occurred significantly before elevations of ICP or change in CPP could be detected. This suggests that CSF pH is a more effective indicator of a patient's neurological condition since remedial action can be taken earlier. It was also noted that measurement of CSF pH provides a means for monitoring cerebral ischemia following blunt head trauma. Falling pH correlates to ongoing cellular injury and occurs well before increases in intracranial pressures.

CLAIMS:-

1. A method of predicting the outcome of head trauma comprising monitoring the pH of cerebrospinal fluid (CSF) with time within the initial 24 hours following trauma.

2. A method of claim 1 wherein a change of CSF pH is monitored within the initial 48 hours following trauma.

3. A method of claim 1 wherein the pH of CSF is monitored with a pH probe received in a ventricle of the patient.

4. A method of claim 1 wherein the measured pH is compared with a base line correlating with brain death.

5. A method of treating head trauma, comprising the steps of:

i. monitoring the change of cerebrospinal fluid pH with time within the initial 24 hours following trauma; and

ii. managing the patient such that the pH rises with time.

6. Apparatus for predicting the outcome of head trauma, the apparatus comprising:

a) a pH probe for reception in a patient's brain ventricle and capable of monitoring the pH of CSF;

b) means for calculating the pH at the probe at sequential times;

c) means for comparing the calculated pH values with stored values; and

d) means for displaying and/or recording the resulting values.

7. The use of the measured changes of CSF pH with time in diagnosis or therapy of neurological injuries.

8. The use of means for monitoring the change of CSF pH over time in the manufacture of apparatus for diagnosing the outcome of blunt head trauma.

9. The use of means for monitoring the change of CSF pH with time in the manufacture of apparatus for the therapy of blunt head trauma.

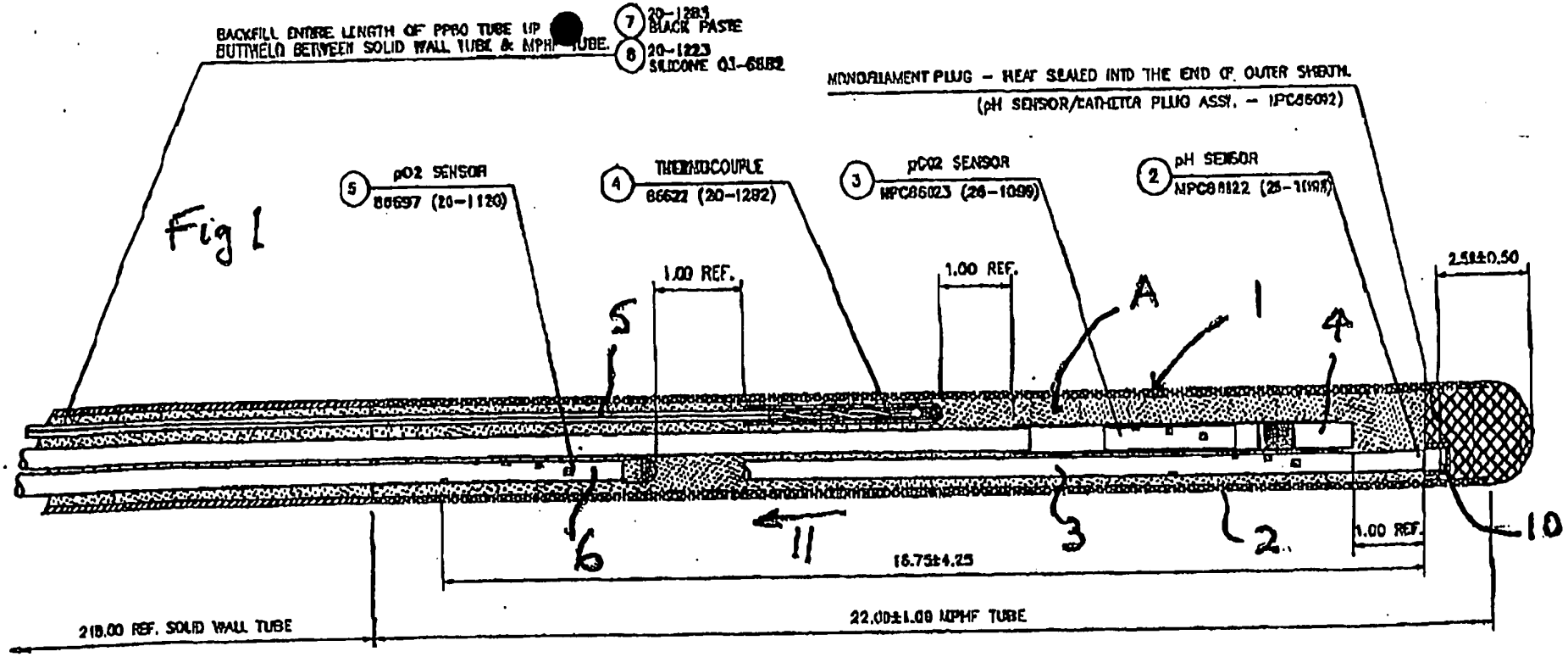

Fig 2

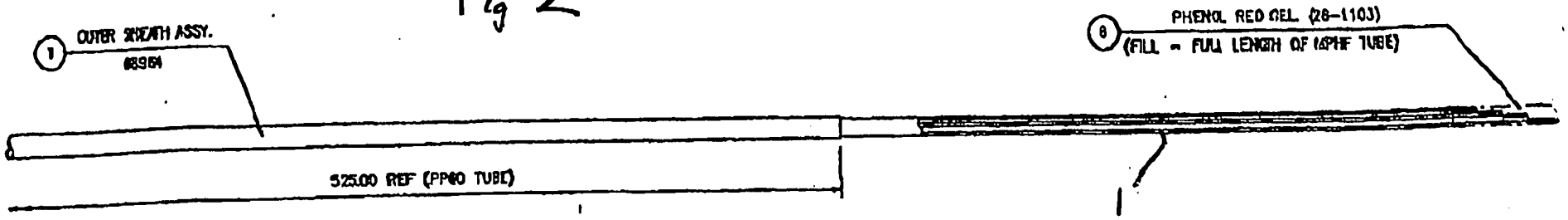

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Fig 3

Figure 3A

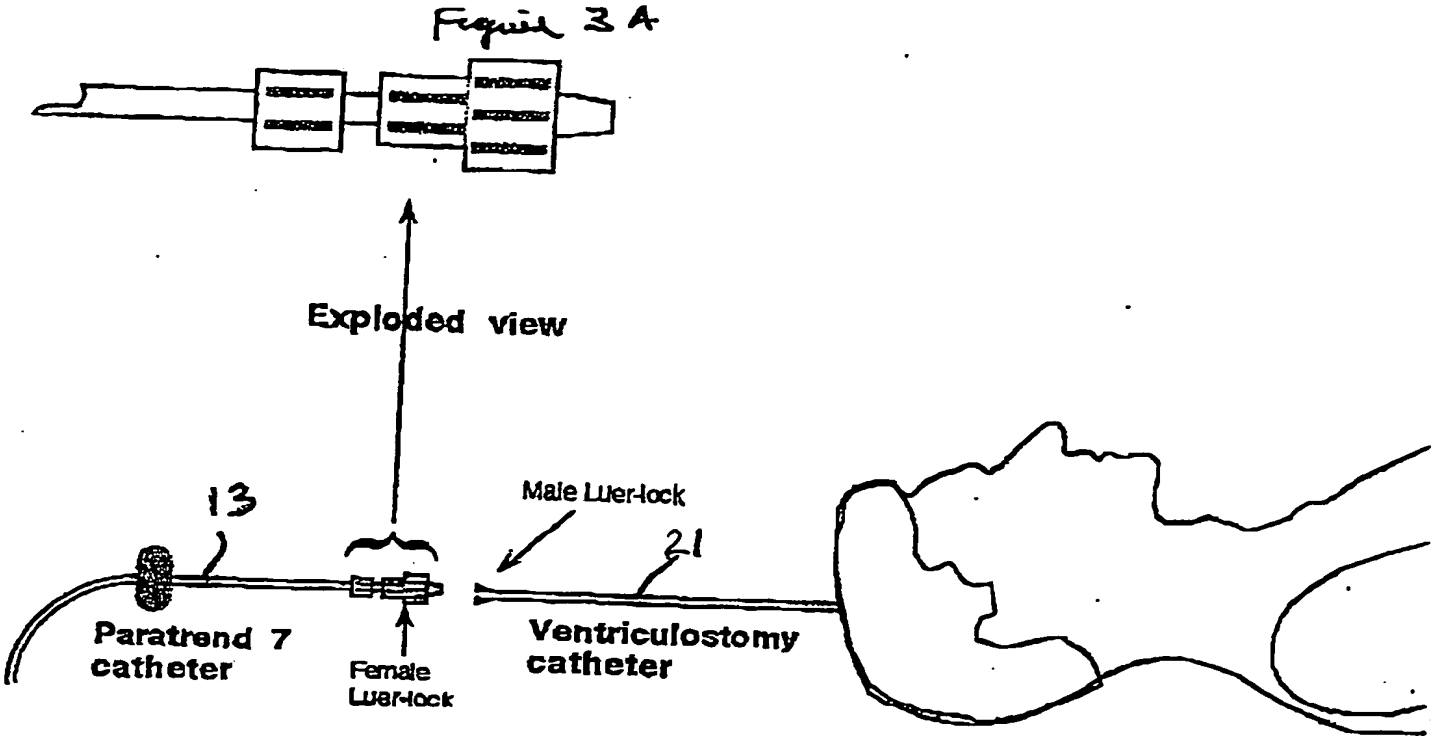

Fig 3B